We claim:

1. A method for expressing a heterologous gene in hepatocytes comprising:

providing replication defective hepadnavirus particles at a titre level competent to infect hepatocytes, wherein a region of the preS or S-gene of the hepadnavirus genome has been replaced with the heterologous gene such that expression of the heterologous gene is regulated by regulatory sequences of the preS or S-gene; and

infecting hepatocytes with the hepadnavirus such that the heterologous gene is delivered into the hepatocytes and expressed in the hepatocytes.

2. The method of claim 1, wherein the replication defective hepadnavirus particles are human hepatitis B virus particles.

3. The method of claim 1, wherein the heterologous gene is inserted into a region of the S-gene such that nucleotides encoding at least one amino acid of the S protein are fused in-frame to the 5' end of the heterologous gene.

4. The method of claim 1, wherein the heterologous gene replaces a region of the S-gene.

5. The method of claim 1, wherein the heterologous gene is inserted after the authentic AUG of the S-gene, and the heterologous gene is inserted such that nucleotides encoding at least one amino acid of the S protein are fused in-frame to the 5' end of the heterologous gene.

6. The method of claim 1, wherein the heterologous gene encodes a modulating agent.

7. The method of claim 6, wherein the modulating agent is a cytokine.

~~8. The method of claim 7, wherein the cytokine is IFNα.~~

9. A method of treating a subject with a hepatic disorder comprising:

providing replication defective hepadnavirus particles at a titre level competent to infect hepatocytes of the subject with the hepatic disorder, wherein a region of the preS or S-gene of the hepadnavirus genome has been replaced with a therapeutic gene such that expression of the therapeutic gene is regulated by regulatory sequences of the preS or S-gene; and

infecting hepatocytes of the subject with the hepadnavirus particles such that the therapeutic gene is delivered into the hepatocytes and expressed in the hepatocytes at a level sufficient to treat the hepatic disorder.

10. The method of claim 9, wherein the hepatic disorder is hepatitis B.

11. The method of claim 9, wherein the hepatic disorder is hepatitis C

12. The method of claim 9, wherein the hepatic disorder is selected from the group consisting of hepatocellular carcinoma, cirrhosis, steatosis, hemochromatosis, and inherited liver disorders.

13. The method of claim 9, wherein the replication defective hepadnavirus particle is the human hepatitis B virus.

14. The method of claim 9, wherein the heterologous gene is inserted into a region of the S-gene such that nucleotides encoding at least one amino acid of the S protein are fused in-frame to the 5' end of the heterologous gene.

15. The method of claim 9, wherein the heterologous gene replaces a region of the S-gene.

16. The method of claim 9, wherein the heterologous gene is inserted after the authentic AUG of the S gene, and the heterologous gene is inserted such that nucleotides encoding at least one amino acid of the S protein are fused in-frame to the 5' end of the heterologous gene.

17. The method of claim 9, wherein the therapeutic gene is a modulating agent.

18. The method of claim 17, wherein the modulating agent is a cytokine.

19. The method of claim 18, wherein the cytokine is IFNα.

20. The method of claim 18, wherein the cytokine is selected from the group consisting of IFNγ, IFNβ, IL-18 and TNFα.

21. The method of claim 9, wherein the hepadnavirus construct is directly administered to the subject.

22. The method of claim 9, wherein the hepadnavirus construct and a helper construct are cotransfected *in vitro* and the infectious particles produced from the culture are administered to the subject.

23. A method of treating a subject with a hepatitis infection comprising:

providing replication defective hepadnavirus particles at a titre level competent to infect hepatocytes of the subject with hepatitis, wherein a region of the preS or S-gene of the hepadnavirus genome has been replaced with a gene encoding a cytokine such that expression of the gene encoding a cytokine is regulated by regulatory sequences of the preS or S-gene; and

infecting hepatocytes of the subject with the hepadnavirus such that the gene encoding a cytokine is delivered to the hepatocytes and expressed in the hepatocytes at a level sufficient to treat the hepatitis.

24. The method of claim 23, wherein the cytokine is IFNα.

25. The method of claim 23, wherein the cytokine is selected from the group consisting of TNFα, IFNβ, IL-18 and IFNγ.

26. The method of claim 23, wherein the replication defective hepadnavirus particle is the human hepatitis B virus.

27. The method of claim 23, wherein the heterologous gene is inserted into a region of the S-gene such that nucleotides encoding at least one amino acid of the S protein are fused in-frame to the 5' end of the heterologous gene.

28. The method of claim 23, wherein the heterologous gene replaces a region of the S-gene.

29. The method of claim 23, wherein the heterologous gene is inserted after the authentic AUG of the S-gene, and the heterologous gene is inserted such that nucleotides encoding at least one amino acid of the S protein are fused in-frame to the 5' end of the heterologous gene.

30. The method of claim 23, wherein the gene encoding a cytokine is a modulating agent.

31. The method of claim 23, wherein the hepadnavirus particle is directly administered to the subject.

32. The method of claim 23, wherein the hepatitis infection is hepatitis B and the cytokine is IFNα.

33. A replication defective hepadnavirus particle, wherein a region of the preS or S-gene of the hepadnavirus genome has been replaced with a therapeutic gene such that expression of the therapeutic gene is regulated by regulatory sequences of the preS or S-gene.

34. The replication defective hepadnavirus particle of claim 33, wherein therapeutic gene is a cytokine.

35. The replication defective hepadnavirus particle of claim 34, wherein the cytokine is INFα.

36. The replication defective hepadnavirus particle of claim 34, wherein the cytokine is selected from the group consisting of TNFα, IFNβ, IL-18 and IFNγ.

37. A pharmaceutical composition comprising the replication defective hepadnavirus particle of claim 33 and a pharmaceutically acceptable carrier.

38. A pharmaceutical composition comprising the replication defective hepadnavirus particle of claim 33 and a helper virus.

39. A method of producing therapeutic replication defective hepadnavirus particles at a titre level suitable for therapeutic use comprising:

co-transfecting hepatoma cell lines with:

(i) replication defective hepadnavirus constructs, wherein a region of the S-gene of the hepadnavirus DNA has been replaced with a gene encoding a therapeutic gene such that expression of the gene encoding a cytokine is regulated by regulatory sequences of the preS or S-gene; and

(ii) a helper construct;

culturing the hepatocytes until infectious viral particles are produced; and

~~recovering the infectious viral particles.~~

40. The method of claim 9, wherein the recombinant hepadnavirus particles administered to the subject are produced by a helper cell line.

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